

Suppl. 10 with its Supplements too.

Mister John G Roberts Jr, Chief of Supreme Court,
1 1st Street, NE, Washington DC, 20543-0002, USA. Paris, 11th July 2006.
From Dr. Y. Zagzyansky, Entraide, 22 rue Ste Marthe, 75010 Paris France

Dear John G Roberts, Chief of Supreme Court of United States ! I must write at level of such famous High Court because of the most Terrible nightmare of Crimes of XXI century at highest all coordinating ExtraGovernmental United States level!

Accusation in Crime Against Humanity. I accuse the most powerful HyperTotalitarian Organization of USA and logically "much much more", ruling de facto The Governmental US Patent and Trademark Office (USPTO) in sure simple intentional atrocious Crime against Humanity and against People of United States: cold assassinations of millions of victims of AIDS with sure projection for continuation of such assassinations because of only one Revolutionary (see his numerous antifascist ISBNs). The proofs are archinett and simple.

By outstanding primitive denagogy of Time of Tribunals of Inquisition and Powerful Hunters of Witches (always alive but adapted and re-coloured to Nights of Humanity and their Good Days), without any obligatory concrete discussion and correction, Governmental USPTO criminally usurped the Elementary Rights of Humanity even to discuss and usurped Law (surely including International one of International Application), rejecting (criminally, openly according to Penal Code) the Application of XXII century with sole means against Pandemic of AIDS and Mad Cow, conducting to cynical Crime against Humanity (possible as unpunished again at their Good Days). By chance for this revolutionary Author (for millions of victims of AIDS and for People of World to realize the Time of Reigning Illegality for the Honest), the USPTO really gave however one sole example (the basis of all rejections!), but which reveals elementary unskilled USPTO Examiners. USPTO Examiners surely stipulated that macrophages do not leave the blood vessels. However elementary for each nowadays student, they DO traverse them for site of infection in tissues. But already this elementary means that USPTO Examiner do not know at all whole field of Molecular and Cellular Biology and Immunology, means of all proofs of Invention, that surely signifies that without doubt, such unqualified "Examiners" could not read the text and made their Demagogy to reject without any sense, any real knowledge, but criminally, like by prepared in advance text for anything! Specially! Penally! Consequently, in connection with millions of intentional victims of AIDS, this is already sufficient for highest punishment of logical Murderers and Assassins = Criminals against Humanity!

Secondly, I accuse United States Government for ArchiBrigandage (many milliards) at intentional stealing (because of certain political convictions of antifascist author) and utilizing

simple clear means against Mad Cow (BSE) of the same published Application (since 2002-2003), avoiding, by rejecting the Patent, to pay milliards as fines for stealing in spite of Crime against Humanity.

You can see all details for exemplary condemnation for open Crime against Humanity in Supplements, wherein in complete openness, I transmit you also my answer to Governmental Responsible of USPTO. Sincerely yours Dr. Y. Zagzyansky

SUPPLEMENTS:

\$1. Concrete details of certain unqualification of USPTO Examiner who surely could not even read Application because of unqualified level.

At elementary idiotic grotesque, appointed (logically by Criminal Ruling Organization in USPTO) Primary Examiner (Mr. Jeffrey Stucker) not only did not read the essential of Patent Application [N°US 10/505,353- National phase of International PCT/EP02/02302 (see yet complete file in USPTO Register by <http://pair-direct.uspto.gov>): "End of AIDS for General Virology, based on profound science as protein foldings: safe vaccines, universal antimicrobial means, mad cow end"], but he a priori surely could not read it with professional understanding because manifestly he is not skilled person and, without doubt, he knew all this perfectly, that is too grave and surely criminal with his such too arbitrary "conclusions".

So de facto, in knowing own absence of any serious possibility for reading and understanding, it is intentional crime to write: all "claims 1-12 (it means all invention) are rejected.. as containing subject matter which are not described in the specification" (it means text) (claims are asked protections: for my new products or processes). And such unlegal global Declarations without concrete discussion but from one of the most prestigious Authority of Governmental US Patent Office had to destroy any answer, any resistance of Revolutionary, because de facto, "normally" this had to be supreme order to all employees of USPTO without any discussion and corrections again. [About such experts and "experts" of American Offices, see book of (measured?) and coordinated? In logical Desert de facto) Known American resisters John Stauber and S. Rampton: "Trust us, We're Experts! How Industry manipulates Science and gambles with your future".

And only due to superchance, "Their Majesties" gave however one "entire"! example (as OverLord's chance for even provability of real arrogant Enemies against Humanity without borders in real camouflaged Desert) and.. it is already more than sufficient certainly to accuse them: it was demonstratively manifestly unskilled man and all written by such man must be also purest intentional falsifications with open 100% Crime against Humanity. "Examiners" wrote: "An example of some unclear, inexact or verbose terms used in the specification are

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W. Stucker for USPTO

(sole "example" and with "are"??? They want to jump as Baron Münch.. or rather from Münch..?): "It is proved that it is only the moving macrophages that are contaminated during movement". It is not clear what is meant by: "only the moving macrophages" because macrophages are in the circulating blood and are always moving".

De facto it is exemplary nonsense. In taking from Fundamental Internet "Web of Science" with ALL best World professional literature for many years only articles (always professional, specialized), which only sole contain even titles with the same (so called "unclear, inexact or verbose terms"): "moving or migrating macrophages or lymphocytes or monocytes", one shall see 10 professional articles of specialists (all with YZ sense) as "Localization of.. proteins in moving macrophages" from Stanford University in Mol.Biol.Cell 7, 2204 (1996). It is already de facto 100% nonsense of USPTO unskilled 1st "Examiner". In taking any presence in Abstract of words: "(macrophage or lymphocyte or monocyte) and (moving and migrating)", one has 944 results!, wherein I saw only the same YZ result! It is already de facto 100%!

But it goes much farther. The macrophages in noncirculating (of course) tissue are not always moving, evidently. So words of "Examiner": "macrophages... are always moving" are complete nonsense, because "Examiner" simply does not know the too elementary: macrophages (leukocytes) can move into tissue from bloodstream.

It clearly proves that such "Examiner" does not know at all Molecular and Cellular Biology and Immunology wherein "The migration of white blood cells out of bloodstream (justly this case) into sites of infection" (text even from Fig.24-15) is known from elementary Manual N°1 for students [Alberts B (President of US Acad. Sci) et al "Molecular Biology of Cell"] (or also classical student Manual "Cellular and Molecular Immunology" Abbas AK, p.255). But even nowadays students in Molecular and Cellular Biology and Immunology, all, know that macrophages traverse the walls of blood vessels for sites of infection. It is incredible revelation of absolute noncompetence of unskilled old fashion Examiner, level of which could choose and find only such sole obstacle of real de facto "understudent"unqualification to cancel by demagogy and unlimited special unpunished power even grandiose series of discoveries of XXII century without any concrete discussion. ANYWAY IT IS ALREADY DONE FOREVER: Examiners without sure possibility of reading with understanding the text (due to sure proven already noncompetence) made Crime against Humanity a priori!

Moreover, all proofs of 101 pages of my very fundamental work with about 900!

References (with the same terms!) for experimental works (Precedent Art) were done with

means of such Molecular and Cellular Biology and Immunology that "Examiner" did not know at all and he must be like clinician of Medicine with surely very old scientific medical bases of 40 years old. It is not "error" of Examiner! It is not to know real: 2 x 2 = 4 and to pretend to teach "Differential Equations" with Crime against Humanity, knowing that "Examiner" even cannot read them!

§2. But "Remarkable" according to even Great Scientists.

This sure crime against Humanity is underlined by leading Scientists. 1st small part of this work (with the same English terms) was not only understandably written but it was estimated as extraordinary by Georges Mathé, President of French Specialized Institute of Cancerology and Immunology (Gold Medal of Academy of Medicine of 2004), Honorary Main Editor of International Journal, author of numerous International Editorials: "With success for your remarkable composition!". And certainly world level specialist of AIDS, chief of laboratory in best Paris University Prof. Zagury even wrote: "Unfortunately I am not qualified to evaluate with utility your work and moreover less to criticize it" (with similar letter of President of National French AIDS Council later). And President of French Acad. Sci. (justly World specialist in Immunology) Jean Hamburger recommended me in Acad.Sci even for immunological Introduction (with English terms) to this work (text published in Publ. FR2711318, p.1).

So it is fantastical: best World specialists of AIDS consider, in 10 Years, the work of author (who is also author of professional publications in "Science", "Nature", "Immunochimistry" etc from best World Institutions where he worked as Inst. Molecular Biology Acad. Sci. USSR with PhD in field, Johns Hopkins University, College de France, Institut Pasteur) much more developed than their own level even for small part of this GRANDIOSE work but unskilled man, who certainly knows too much less than leading Prof.Zagury, reject titan work, that he certainly (see above) could not even read. And it is with sole possible solution of Epidemic of AIDS, that this logically Ordering Criminal Totalitarianism must also know. But it is blaspheme of any existence of Civilization, it is Hymn to victorious Enemies of Humanity and I accuse this Totalitarianism and its Executor who must be (all) exemplarily punished! (See details in Supplement as justly finished works: as "To stop tragedy Human at Horror of well underestimated Pandemic: all searched means against AIDS are scientific nonsense, except sole basic ignored solution")....

§3. All it certainly looks as Strategy of one World Totalitarian Organization to cut Revolutionary by any way!

Y. P. P. for USPTO

This is National US phase of International Application wherein Determining Examination (Search) was done already by International Search Authority (ISA) (European Patent Office-EPO in this case) that governs (see: obliges) the global work of Examiners at National Phases. EPO makes the same Examination at International phase for USPTO too.

So globally, USPTO National Examiner is obliged to do nothing serious [moreover, the same Examination, EPO (ISA) had to make for USPTO too!]. Moreover, EPO and USPTO signed "Memorandum of Understanding" about "harmonization or standardization of Search strategies and substantive Patent Law". And justly EPO (ISA) terribly made this Examination with proven falsifications wherein globally EPO did not examine a number of claims because they are "scientific theories" (it means: precise, solid) and did not examine therapeutic processes (with patentable products). These formal illegal (see: even criminal) things were easily and clearly destroyed by me, especially in last answer (10/22-27/2005) (see EPO Register: www.epo.org, later Epoline and Register). But even in spite of intentional falsifications! and intentional attempts (complete fiasco after my answers) to destroy Patent, EPO wrote nothing that now USPTO "Examiner" proclaimed NEWLY. It again confirms impertinent arbitrary of Totalitarian System wherein moreover "scientific theory" means precise, solid confirming again intentional crime of Demagogy of empty words.

EPO has the problems to answer: too open Crime against Humanity can be very heavy! So as the same Totalitarian Criminal Organization, USPTO does not take these destroyed (but not answered during 8 months by EPO) precise arguments that USPTO must follow... In such situation, for obvious effectivity, I sent Fax (11/28/2005) (receipt N°FA1-03-55953) in asking to suspend action for 6 months to wait ISA (EPO) determining International answer. But, very strangely, there is no such Fax in file??? (in spite of parallel e-mail) wherein another Fax (N°FA1-03-55964) from the same post and time is in the file of my other application (10/508,967). So with this intentional (as I think) disappearance, USPTO Organization justly began new type of Campf: unconcrete Demagogy which is undiscussible. Only by chance of sole example, revealing surely complete absence of corresponding level to read, I proved intentional Crime against Humanity! EPO obligatory answer must confirm it, especially after accusation in Brigandage with stealing and using the means against terrible Mad Cow by European Governments, that European Court justly shall see.

§4. Appointment of "Examiner" Jeffrey Stucker: is he one of special pertinent agents of Criminal Totalitarianism, really Ruling Organization in USA and the Rest?

But how expressively incompetent unskilled Examiner received this file? File was received by Technology Center 1600 and its Department 1640: "Immunology, receptors/ligands...

Molecular Biology" and directed to this Art Unit 1648. And how Chief of this Unity Mr. Bruce Campbell transmitted it to unskilled (but special!) man? Is this special man who wrote terrible Demagogy of Crime against Humanity and who can take what he want after his received criminal task? What interests he had "to examine" such work, wherein his level does not permit even to read text! It is important problem: who really gives order in USA: agents? And Supreme Court?

Such strange appointment and Totalitarianism were demonstrated even in my 1st USPTO Application (1988). Examiner Jeff Kushan made complete exemplary Search (although I was complete Novice before tens and tens Applications). He sent me two Patents as simple matrices to correct form of already very positive searched claims, that I very simply did. But suddenly such my answer arrive not already to J.Kushan but to another person (Marg. Moskowitz), who denied already recommended and done! And no letter from already positive Examiner Kushan. Later I received "Notice of abandonment" that I did not answer for letter of 12-19-88 that I never received (logically from Mr.Kushan). Any my letters to USPTO to have this "abandoned" not received letter were without any (any!) answer. It was loss of millions of litres of human blood with... similar principle as working Mad Cow! Is it not Open Brigandage of Governmental Office ("Democracy in Action") against Revolutionary even at already done principally Patent? The same appointment of special man, ready to do everything for Totalitarian Organization?

It means from beginning USPTO made the exemplary Examination even for complete Novice of my 1st Application of 1988. But when I made English terms Application (PCT/IB00/00843) in new for me field of global Theoretical Physics (wherein I do not have PhD, experience in best World Schools, 30 publications in best International journals), moreover with proven End of Einstein-Bohr Physics, the Dutch (Foreigner) Examiner Mr.Capostango understood all and made complete positive even exemplary Search (with all serving terms in New discussible science). It is, otherwise de facto complete intentional political demagogy of English speaking Totalitarian Organization without Law! It is too obvious nonsense! To stop it!

§5. Totalitarian Criminal Network of all World Science logically participate in atrocities of Crime against Humanity because of only one Revolutionary!

But is it impossible, it is too much, Dr.Zagjansky! Of course too much! And to prove such criminal Infernal Machine against Humanity (with fantastical Theatre of Solid-like Magicians-Actors: "Trust us, we're Experts") is really impossible except the same chances!

Vukobratovic
for USPTO

Cancer! Antiretroviral Therapy HAART (Highly Active, moreover) can stop division of cancerous cells and Medicine utilizes HAART to stop cancers at AIDS. But they all do not use it at all against all other cancers with this evident idea, moreover published very knowingly. So logically Big K^c knows that HAART is too dangerous and they can "fantastically" arrange that nobody uses it.

So they claim everywhere the success of highly active HAART (see Fig. 4 from Fauci AS et al Emerg Infect Dis 11, 519, 2005 and Fig. 1b from Weiss RA Nat Med 9, 887, 2003), logically only to make appearance that situation is not so tragic. And consequently sole means against AIDS can be however stopped without special danger (as openly by USPTO). Moreover, in written detailed article: "HAART must signify Highly active ART to kill and has to be stopped urgently: Evident proofs" (for submission), I confirmed such prudent fear of logically knowing Criminal Totalitarianism!

There is Special overpowered Network that makes plans and executes political persecutions of honest Resistant-antifascists. It is impossible to prove it as nett. But there is clear sure case. Already after two years after University, I made world discovery (confirmed) and was cited by very famous scientist (C.Tanford) in best mondial Review (Dorington and Tanford, Adv Immunol 12, 333, 1970) for about one page!! But in famous "Science Citation Index" ("Web of Science"), one will not find such important citation of our article (Zagzyansky et al Immunochimistry 6, 787, 1969). It is sure de facto Mondial political Spider Web: K^c eliminated, from Internet, the citations of justly articles of Advances in Immunology (best reviews, only several for year! It is impossible) around 1970 but they had to leave more ancient citations from this journal with Nobel Winners!... It confirms real Industry of political persecutions in Science.. and in Patent Offices, evidently, surely, criminally, even with sure falsifications at intergovernmental level!

§6. Preliminary Accusation of United States Government in intentional stealing and robbery of preparation against Mad Cow [Appl. US 10/505,353 (PCT/EP02/02302)] with covering it by certain intentional falsifications to cut said Patent.

After book of 1997, "Mad Cow USA" written by known official Resistant in USA (measured?), characterized as "[the authors] have done the legwork and research necessary to produce a solid accounting of the affliction of mad cow disease" ("Chemical & Engineering News, 04/20/1998), the real announcement of disease by US Government (12/23/2003) reveals the presence of very probable even Epizootic in USA, especially in situation wherein even known means of spreading were not forbidden in USA. Only defence of meat and bone meal (made from killed cattle and used to feed the new animals) in France costs 6 milliards of

Euros ("Impact Medicine" N°166, 06/22/2006, see here) (it means about 80 milliards of \$ in USA).

.... The situation at 2002 was tragic in Europe (data more accessible according to above book too). "The number of cases continues to increase in the UK" [Review, Ghani AC Microb Infect 5, 385, 2002]. "In 2003 (work was made in 2002) in an updated study Fergelson and Donnelly... estimated that 400000 (which even scale!!!) British cattle has been infected by BSE" [Supervie V C.R.Biologies 329, 106, 2006]. And vigilance was extraordinary: "It is unadmissible that 10 years after their ban, the traces (EVEN!) of meat and bone meal can be found in feeding of bovines... I do not ignore economical and technical problems... However the case of elimination of meat and bone meal and of systematic screening must be fixed..." French President Chirac (10/25/2000). However this crisis costs 90 milliards of euros to Europe... Pessimism reigned for many years....

And suddenly the Miracle! In March of 2006, embargo for British meal is removed! In May of 2006, there is re-introduction of fish meal (contaminated usually with cattle meal) must be done. (That was justly recently banned as "serious problem which may prolong the BSE epidemic" according to European Scientific Committee). "European Government ("Commission") programmes the return of meat and bone meal in 2 years" ("Impact Medicine", N°166, 2006), that was justly demonstrated as the most dangerous in Epizootic [Baron T Pathol Biol 53, 229, 2005]. Fantastical! Now ALL, with animals, are becoming Crazy!...

But how does it happen? With Dr.M.Eliaszewicz (Chief of French special State central Commission for Control), everyone see only the same used means as defence of suspected animal meals and systematic screening. But justly at the end of 2002, my this great Application was published. To synthesize miraculous peptides (small protein "Du-2T" of prion of appr. 20 amino acids) is routine and invisible as we see here de facto too (in reality logically by the same PROVEN falsifiers of Governmental Offices!). Let's see. Before: "when a case of BSE is identified, the entire herd is usually slaughtered". And NOW:

"animals which appear to be healthy could be used until end of their lives" ("Environment" 04/25/2006)! And why else, except such simple Miracle! Of course, surely, only if easily to inject such peptide [YZ US 10/505,353 (PCT/EP02/02302)]... So logically, only in such already solved and "used" situation, US Government admitted justly, at the end of 2003, "one" case of Mad Cow in USA. And of course, as in Europe: now the embargo for US meat is removed in Japan and other countries! All is o'key... We can see other proofs. All proven international falsifications by European Patent Office were done without any border between

Y. Zagzyansky for USPTO

Nationalities of EPO employees, as one Spinder's Overgovernmental Organization of course with Great known USA Totalitarian dominating SuperOrganization, as we see in common systematic Brigandage of Superpatents of Revolutionary Antifascist (see his ISBNs de facto) even with accusation in Crimes against Humanity. (They simply play game with resistants-dissidents as "cat with mouse": which "democracy" with "Posts" and "Times"!).

But there are strange cases. According to European Statistics (that of course, in such situation, could be more "imaginative"), a number of cases of Mad Cow (BSE) sharply decreases in UK and France, but oppositely it increases in New East European members (Poland, Czech Rep.). Of course, Old (see my Historical books) Totalitarian Criminal Organization does not believe yet (it needs more [known to them] spread corruption etc for complete slaving) to new members in Common Crimes as Governmental! Stealing! "The European Government discusses about removing of means for precaution without asking opinion of Authority of Food Security" (ELSA)", Dr. Eliaszewitz worries ("Impact Medicine" ibid). And Why? Justly there are de facto East European members in such Authority and they (ancient Socialist countries!!!) yet do not participate in Common Crimes: to avoid!

Sure action of preparations will be surely confirmed experimentally = stealing for 99,999% and "The Supreme Court" would be as Guardian of Brigands and Assassins of Jungles of Witches.

So I transmit to Supreme Court of USA Accusation to stop Crime against Humanity of US Governmental Patent Office (USPTO) and preliminary accusation about US Government stealing of means against Mad Cow. Sincerely yours Dr.Y.Zagyansky

Supplements: 1. Answer to USPTO of 07/10/2005 with all its Supplements. 2. Copy of **Exemplary Complete Search made yet in 1988** by USPTO even for my much less formally developed 1st Patent Application. 3. "Notice of Abandonment" (09/18/89) due to letter of USPTO of 12/19/88 (as unanswered), that I never received (and could not receive in spite my numerous letters to USPTO without any answer). 4. Fig. 4 of Fauci et al Emerg Infect Dis 11, 519, 2005 and Weiss RA Nat Med 9, 887, 2003 5. Copies from "Web of Science": a) Citing of article: Zagzyansky et al Immunochimistry 6, 787, 1969 at page where the citation by Dorington and Tanford Advances in Immunology 12, 333, 1970 had to take place (but missed); b) Source Index: page with articles of "Advances in Immunology" with jump, logically too specially, from 1976 to 1964 (justly without 1970) that led to absence of JUSTLY exemplary citation by grand Tanford (and Dorington). 6. Long text of grand citation (by famous Prof. Tanford) of Zagzyansky et al 1969 (grand independent discovery,

already 2 years after University). 7. Confidentially, the text of justly written article: "To stop Tragedy Human of Horror of well underestimated Pandemic: all searched means against AIDS are scientific nonsense, except sole basic ignored solution" (without 2 lines of p.2) that will be sent together with articles: "Antiretroviral Therapy- "HAART" must signify Highly Active ART to kill and has to be stopped urgently: evident proofs" and necessary basic: "Errors of heart of Immunology: completely erroneous general structure of main receptors and Principal Scheme of Immunology" that will be sent to Prof.Mathé's journal (by himself as Founding Editor of his International Journal in such too special case). 8. "Impact Medicine" N°166, 06/22/2006, pp.6, 8.

Y. Zagzyansky for USPTO

AUGUST 1987

Suppl. 2 (To Cont.)

exp. USPTO

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183

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NOTICE OF REFERENCES CITED

APPLICANT(S)

Zagyan sky

U.S. PATENT DOCUMENTS

* A	DOCUMENT NO.	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE
A	4661586	9/28/87	Levy et al	530	388	11/17/81
B	4690893	9/1/87	Mosmann	530	387	5/3/85
C						
D						
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OTHER REFERENCES (Including Author, Title, Date, Pertinent Pages, Etc.)

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7/12/88

* A copy of this reference is not being furnished with this office action.
(See Manual of Patent Examining Procedure, section 707.05 (a).)

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SERIAL NUMBER	RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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07-175-487 11 02 88 ZAGYANSKY

Y. ZAGYANSKY
18 RUE DE TOLSTOY
75013
PARIS, FRANCE

DATE MAILED: 09-18-88

NOTICE OF ABANDONMENT UNDER 37 CFR 1.53

Regarding the Notice to File Missing Parts, dated 12-19-88, no response was received.

Therefore, the above identified application is ABANDONED.

Note: When an application is abandoned for failure to pay the filing fee, the application will not be retained (i.e., the application papers will be disposed of) copies of the application will not be provided or certified, and benefits under 35 USC 120 and 37 CFR 1.78 will not be accorded unless the processing and retention fee set forth in 37 CFR 1.21(1) is paid within the one year period set forth in 37 CFR 1.53(d).

A petition to the Commissioner under 37 CFR 1.137(a) may be filed requesting the application to be revived.

Under 37 CFR 1.137(a), a petition requesting the application be revived on the grounds of unavoidable delay must be filed promptly after applicant becomes aware of the abandonment and such petition must be accompanied (1) by an adequate showing, verified under oath or declaration, of the cause of unavoidable delay, (2) by the required response to the above identified Office letter, and (3) by the petition fee set forth in 37 CFR 1.17(1).

37 CFR 1.137(b), (unintentional delay) does not apply to revival of applications abandoned under 37 CFR 1.53(d) for failure to complete an application.

Any questions concerning petitions to revive should be directed to Petitions Information. (703) 557-4282.

Musha Smith
Special Processing Branch
ONIA, Application Processing Division
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Yu Pan



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Volume 11, Number 4, April 2005

Emerging Infectious Diseases: a 10-Year Perspective from the National Institute of Allergy and Infectious Diseases

Anthony S. Fauci,* Nancy A. Touchette,* and Gregory K. Folkers*
*National Institutes of Health, Bethesda, Maryland, USA

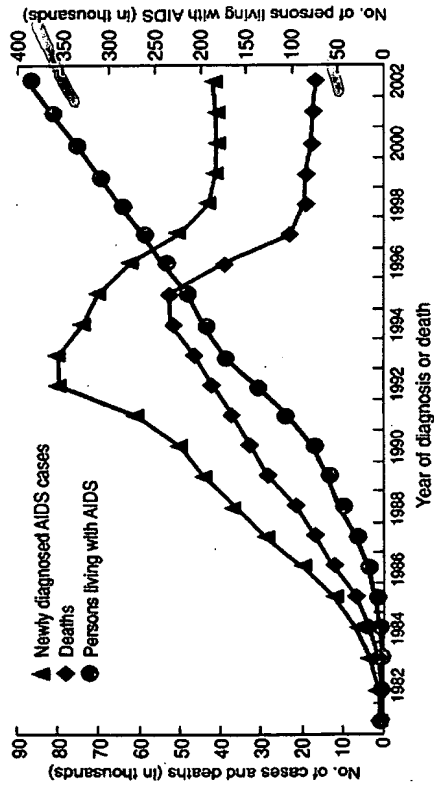


Figure 4. AIDS cases, AIDS deaths, and persons living with AIDS in the United States, 1981–2003. Over the past decade, the number of new AIDS cases and deaths due to AIDS has decreased, while the number of people living with the disease has increased, due in large part to improvements in diagnosis and treatment. Estimates adjusted for reporting delays. Source: CDC (8).

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This page last reviewed March 14, 2005

**Emerging Infectious Diseases Journal
National Center for Infectious Diseases
Centers for Disease Control and Prevention**

Variation in HIV: evolution or noise?

On June 10, 1964, the following was received from the Bureau of the American Medical Association:

NUMBER 7 | JULY 2003 | NATURE MEDICINE

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FLEXIBILITY OF IMMUNOGLOBULIN G MOLECULES AS ESTABLISHED BY FLUORESCENT POLARISATION

MEASUREMENTS

ZAGYANSKAYA, NEZLIN RS, TUMERMAN LA
IMMUNOCHEMISTRY
6: 787-8 1969

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☐ 41. ZAGYANSKAYA, TUMERMAN LA, EGOROV AM
SEGMENTAL FLEXIBILITY OF IMMUNOGLOBULIN-M MOLECULES
IMMUNOCHEMISTRY 9 (1): 918-1972
Times Cited: 8

☐ 42. TUMERMAN LA, NEZLIN RS *ZAGYANSKAYA*
INCREASE OF ROTATIONAL RELAXATION-TIME OF ANTIBODY
MOLECULE AFTER COMPLEX FORMATION WITH DANSYL-HAPTEN
FEBS LETTERS 19 (4): 2908-1972
Times Cited: 23
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☐ 43. BJORK I, TANFORD C
GROSS CONFORMATION OF FREE POLYPEPTIDE CHAINS FROM
RABBIT IMMUNOGLOBULIN-G.1. HEAVY CHAIN
BIOCHEMISTRY 10 (8): 1271& 1971
Times Cited: 50

☐ 44. YGUERABI J, EPSTEIN HF, STRYER L
SEGMENTAL FLEXIBILITY IN AN ANTIBODY MOLECULE
JOURNAL OF MOLECULAR BIOLOGY 51 (3): 573& 1970
Times Cited: 344
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☐ 45. NEZLIN RS, ZAGYANSKAYA, TUMERMAN LA
STRONG EVIDENCE FOR FREEDOM OF ROTATION OF
IMMUNOGLOBULIN-G SUBUNITS
JOURNAL OF MOLECULAR BIOLOGY 50 (2): 569& 1970
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19/06/2006

Molecular size and conformation of immunoglobulins.

Dorrington K.I. Tanford C.

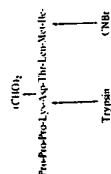
MOLECULAR SIZE AND CONFORMATION OF IMMUNOGLOBULINS 345

molecular dimensions obtained from other measurements, when interpreted in terms of a rigid ellipsoid, a value near 220 nsec. would have been anticipated. Indeed, measurements of the rotational relaxation time for horse γ G by dielectric dispersion (Onley, 1943) and human γ C by electric birefringence relaxation (Krause and O'Konski, 1965) have given values of 220 and 200 nsec, respectively. Electric birefringence studies on bovine γ C gave rotational relaxation times of 215 nsec. (Ingram and Jerrard, 1963.) The discrepancies in the relaxation times provided by fluorescence depolarization measurements and other methods was interpreted to mean that different regions of the γ C molecule could rotate independently; a situation which could be envisaged in the Noelken *et al.* model.

More recently this interpretation of the fluorescence depolarization data has been challenged (Weltman and Edelman, 1967; Wahl and Weber, 1967). These workers suggest that thermally activated rotations of the covalently bound DNS groups can occur independently of the rotation of the region of the molecule to which they are attached thus leading to low values for the rotational relaxation time of the protein. The use of fluorescence depolarization to determine molecular relaxation times depends on the requirement that the fluorescent label should be immobilized by strong interactions with the protein molecule. Weltman and Edelman (1967) and Wahl and Weber (1967) showed that the slopes of the fluorescence depolarization curves obtained isothermally at varying viscosities (sucrose isotherms) are smaller than the slopes obtained when the temperature is changed to alter the viscosity of the solvent without sucrose. Values of the rotational relaxation time calculated from sucrose isotherms at different temperatures ranged from 191 to 244 nsec., whereas heating curves gave values below 100 nsec. in agreement with earlier studies. These results seemed to indicate that under experimental conditions where free rotation of the dye molecules is minimized, values of the rotational relaxation time can be obtained from fluorescence studies which are apparently consistent with values obtained by other methods and previously calculated molecular dimensions. This does not appear to be the whole story according to a recent paper by Zagaynsky *et al.* (1969). The latter have shown that dimethylaminonaphthalene sulfonyl chloride (DNS) conjugates of human and rabbit γ C have different fluorescence properties from DNS conjugates of serum albumin and ovalbumin. Of particular relevance was the finding that the lifetime of the excited state for DNS γ C was shorter (7.3 nsec.) than for DNS albumin (12.1 nsec.). Since the value of the lifetime of the excited state (τ) is required in the depolarization calculations, exact knowledge of it is of great importance. Zagaynsky *et al.* (1969) calculated the rotational

Zagaynsky, Y. A., Neelin, R. S., and Tumennan, L. A. (1969). *Immunochemistry* 6, 787-800.

extended portion con-
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tsumi (1967) and of
defined the cleavage
onide (Fig. 2). The
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an of rabbit γ C-globulin
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relaxation times of the DNS γ C to be near 60 nsec. using sucrose isotherms and $\tau = 7.3$ nsec. Recalculation of the data of Weltman and Edelman (1967) and Wahl and Weber (1967) gives values of 100 to 130 nsec. using the lower lifetime value. The even lower value of 60 nsec. obtained by Zagaynsky *et al.* may have been due, in part, to their removal of aggregates from the DNS γ C preparations before the fluorescence measurements. These authors also provide some experimental evidence that the shorter lifetime of the excited state in DNS γ C may be explained either by the substitution of DNS onto different amino acid side chains, the alternative conjugates having different spectral properties, or by differences in the hydrophobic nature of the environment of the DNS groups between DNS γ C and DNS BSA. DNS-aspartate transaminase seems to have similar fluorescence lifetime properties to DNS γ C (Polyanovsky *et al.*, 1970).

It seems from the above discussion that, even allowing for free rotation of the dye molecules, the rotational relaxation time for DNS γ C is lower than expected for a rigid molecule. Thus it would seem that the units of the γ C molecule with some rotational freedom are smaller than the whole molecule, and it is tempting to suggest that they correspond to the Fab and Fc fragments.

Two recent papers have reported fluorescence polarization measurements by direct measurement of the relaxation process (time span in the nanosecond range) following excitation by very short light pulses. This technique is free from some of the ambiguities that apply to previous results obtained by steady state measurements under constant illumination. Wahl (1969) employed DNS γ C, with the DNS coupled covalently to the protein. His results were analyzed in terms of two relaxation processes, with relaxation times of 370 and 23 nsec. The first, which accounts for 65% of the overall relaxation process, is ascribed to rotation of the whole molecule and the second to internal Brownian movements of a globular region of the molecule. (The relaxation time, however, is much too short to represent a globular region of the size of the Fab region of the molecule.)

The second paper using the nanosecond fluorescence technique is by Yguerabide *et al.* (1970). They coupled the DNS chromophore to γ C noncovalently by using γ C that was an antibody directed against it. They also observed two relaxation times, one of 500 nsec., which is of the same order of magnitude as Wahl's longer relaxation time. The shorter relaxation time, however, was found to be 100 nsec., i.e., four times as large as Wahl's. When the same measurements were carried out with the complex between the DNS hapten and the Fab fragment of the antibody, only a single relaxation time of 100 nsec. was observed. The 100 nsec. relaxation

Polyanovsky, O. L., Zagaynsky, Y. A., and Tumennan, L. A. (1970). *Mol. Biol. USSR*

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Des études à conduire. La crise de la vache folle a entraîné 80 millions d'euros d'Europe

Des études à conduire. La crise



Dix ans après la crise et alors que le nombre de cas d'ESB est en baisse, l'Europe envisage déjà de réintroduire les farines animales... pourtant à l'origine de l'épizootie. La Commission européenne programme leur retour d'ici à deux ans. L'AFSSA exprime de fortes réserves.

VACHE FOLLE

POLÉMIQUE SUR LE RETOUR DES FARINES ANIMALES

Mars 1996: l'Europe et le monde découvrent avec effroi que l'encéphalopathie spongiforme bovine (ESB) pourrait se transmettre à l'homme; dix cas atypiques de la maladie de Creutzfeldt-Jakob ont été recensés en France. Les ventes de viande bovine s'effondrent.

Dix ans après cette crise alimentaire sans précédent, le danger semble écarté... et l'Europe parle déjà de réintroduire les farines animales. Pourtant, les scientifiques qui sont incriminés depuis la sécurisation des farines de viande et d'os (FVO) en 1996 et

l'interdiction totale en Europe au début de 2001, la prévalence de l'ESB a diminué. L'exemple français est éloquent. En 2001, 3,5 cas d'ESB ont été déclarés pour 100 000 tests réalisés à l'abattoir, contre 0,5 cas en 2005.

Une ouverture progressive des verrous. Devant cette baisse et le succès des mesures adoptées, l'heure est venue de réévaluer l'assouplissement. Par exemple, l'Europe parle déjà de réintroduire les farines animales. Pourtant, les scientifiques qui sont incriminés depuis la sécurisation des farines de viande et d'os (FVO) en 1996 et

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suite de la page 4

Chiffres clés en France

- 980 cas d'ESB depuis 1991
- 17 cas liés au nouveau variant de la vache folle
- 170 000 tonnes de farines animales entrées en France au 31 décembre 2005

Pas de risque zéro

Mais si le test de détection chez les bovins doit permettre en théorie d'éviter la chaîne alimentaire d'être contaminée, elle ne vient confirmer cette crainte. La modernité agricole tendrait pour expulser et recevoir les ingrédients autorisés et probables s'est élevée à l'origine de la contamination.

Par ailleurs, si la crise a permis de faire progresser les connaissances sur les maladies des animaux, il est probable que des animaux malades passent au travers des mailles du filet, notamment à l'exportation.

Direction générale de l'alimentation, et enfin par l'ESB (trois cas suspects signalés), « il existe trop d'incertitudes pour prendre des mesures de gestion à l'égard », conclut le Dr Eliazewicz.

Dans tous les cas, si une telle décision est prise en Europe, la France, en théorie, devra s'y plier.

JEAN-PIERRE BARRESI et MARIE DORNEY

« Les outils d'analyse sont aujourd'hui plus performants, et nous avons les moyens de mieux contrôler les farines animales. Le risque de contamination est donc minime. »

ELIE ANGLAN, chef du service de sécurité et de qualité alimentaire au sein de l'INRA (Union européenne)

« Le nombre de cas liés au variant de la maladie de Creutzfeldt-Jakob (vMCJ), qui est la forme humaine de l'encéphalopathie spongiforme bovine (ESB), ne représente qu'une infime partie des cas d'ESB recensés. En France, 185 cas de vMCJ ont été déclarés en 2000, contre 100 cas en 1996. La France a donc une incidence plus faible que la moyenne européenne. »

Philippe Barrot, chef de la cellule nationale de référence des maladies de Creutzfeldt-Jakob et à l'Institut Pasteur, explique que la vache folle est une maladie à l'origine de la contamination.

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Dr. CLAUDE BRONNER, président d'Espèce Cœur

Unions: la bat

Comme prévu, l'élection syndicale à l'été prochain sera l'occasion pour les syndicats de la santé de se réunir et de discuter de la présidence de l'Union nationale des syndicats de la santé.

Le « deuxième tour » promet d'être intéressant. Les syndicats de la santé ont des positions très divergentes sur la présidence de l'Union nationale des syndicats de la santé.

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